UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,696	09/19/2003	Ulrich Feige	A-527H	8548

7590 05/04/2005

US Patent Operations/[TJG]
Dept. 4300, M/S 27-4-A
AMGEN INC.
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

EXAMINER
WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/666,696	FEIGE ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,63 and 64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,63 and 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 1-7 and 63-64 are pending in the application and under examination.

Claims 8-62 have been cancelled.

Withdrawn Objection and Rejection

In view of the amendments to the disclosure and a new abstract on the record, the objection to abstract of the disclosure is withdrawn. Also, withdrawn are the 35 USC 112, second paragraph rejection, in view of applicants' arguments and the obviousness-type double patenting over copending Application No. 09/563286 in view of the terminal disclaimer of record.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-7 and newly added 63-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention for reasons advanced in the last Office action.

Response to Arguments

Applicants state that the rejection fails to consider the definition of "randomized" (page 21, lines 8 to 15). The Examiner appears only to consider sequences derived from natural sequences and not those sequences obtained from random peptide library screening (e.g., phage display).

In response, applicants however fail to point out support for the present claimed, "Randomized ***Ang-2 binding peptide***".

The Applicants note that the specification provides ample teaching on how such technologies can be used to generate peptides and how such peptides can be used to form Fc fusion molecules. The working examples (pages 91 to 131) provide numerous examples of peptides directed at targets other than Ang-2. The Examiner has cited no reason to doubt that these teachings will not be applicable to peptides that bind Ang-2.

In reply, a claim to Ang-2 binding peptide should describe said Ang-2 binding peptide and not other targets to which a peptide binds thereto. The law is clear in its requirement that at the time the application was filed, applicants had possession of the claimed invention. Thus, reference to other numerous

examples of peptides except that, which is claimed, is not a description of the claimed Ang-2 binding peptide.

Applicants state that in Enzo the court quoted with approval from the MPEP Guidelines wherein it is alleged that the PTO has determined that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." For example, the PTO would find compliance with 112, P1, for a claim to an "isolated antibody capable of binding to antigen X," notwithstanding the functional definition of the antibody, in light of "the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature." Synopsis of Application of Written Description Guidelines, at 60.... The Enzo court then applied these principles to the claims of the patent in suit. The claims therein concerned antibodies defined by the functional characteristic of preferential binding to N. gonorrhoeae over N. meningitidis. The court found that the

written description requirement was met because the functional characteristic was coupled with "a structure that is sufficiently known or disclosed." The presently claimed Fc-peptide fusion molecules are analogous to the antibodies of Enzo. Claim 1 includes the structural formula, satisfying the "partial structure" mentioned in the Guidelines and cited in Enzo. The Fc domain, which is specified in the structural formula, makes up most of the structure of the claimed molecule, compare, for example, the Fc domain of SEQ ID NO: 2 with the peptides appearing in the working examples. In Enzo, the term antibody supplied sufficient structure that, coupled with the functional characteristic, it satisfied the written description requirement. In the present application, the structural formula supplies sufficient structure that, coupled with the functional characteristic, it satisfies the written description requirement. Furthermore, the present specification provides even greater written description than the specification in Enzo. This point becomes stronger as the structure becomes more detailed, as in Claims 3 and 4. Like Claim 1, these claims present structure with even greater specificity than attended by the mere use of the word "antibody," which the Enzo court found sufficient.

In reply, the instant case is inapposite to the guidelines in MPEP. Random peptide that binds to Ang-2, as defined at page 21, lines 8-15 refers to "peptide sequences [which] refers to fully random sequences (e.g., selected by phage display methods) and **sequences in which one or more residues of a naturally occurring molecule is replaced by an amino acid residue not appearing in that position in the naturally occurring molecule**." (Emphasis added). Accordingly, it is not seen how a random peptide is considered a well-defined structure when it is a random sequence. There is not a single known sequence for said sequence to be randomized let alone its binding to Ang-2, especially since said Ang-2 is not described in the specification as of the filing date. While Fc is defined in the claims however, the claims are not drawn to Fc alone. Rather to a complex comprising known and unknown components. Fc is not involved in binding but functions as a carrier for the random binding peptides.

Applicants further argue that claims 63 and 64 also provide clear written description. In these claims, the peptide portion of the claimed structure is defined in the form of a product by process. The patent law has long held that product-by-process claims satisfy the requirements of Section 112.

In response, a product defined by the process by which it can be made is still a product claim (In re Bridgeford, 357 F.2d 679, 149 USPQ 55 (CCPA 1966)). These claims does not recite a product by process rather products by processes. The claims recite numerous different methods for which not a single method has been applied to the present product claim. Thus, it is not evident from the disclosure which method from the numerously recited ones has been employed that results in a peptide that binds to Ang-2. The Eli Lilly case appears applicable here. Applicants are seeking to sweep in all products produced by all the methods without a single showing for the species of Ang-2. Rather than describing the single claimed Ang-2 binding peptides species, it describes numerous unrelated targets (orthologs from all mammalian species, as in Lilly). In Eli Lilly, the court found that such a claim breached the written description requirement of Section 112 and cited structure, formula, chemical name as examples of suitable written description.

Claim Rejections - 35 USC § 103

Claims 1-7 and 63-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cerretti et al (WO 00/75323) for reasons set forth in the last Office action.

Response to Arguments

Applicants state the Tek antibodies bind to Tek rather than to a Tek ligand such as Ang-2. Thus, Tek antibodies have a different mechanism of action from the ang-2 binding molecules of the present invention. As there are other ligands for Tek, such as ang-1 (page 2, line 35), one of ordinary skill in the art would expect this difference in mechanism to lead to different biological activity.

In response, applicants' arguments are not commensurate in scope with the claims, as the claims do not recite for a mechanism. Rather a composition comprising of an Fc domain and a random peptide that binds to Ang-2, which composition is taught or at least suggested by Cerretti.

Applicants argue that the degenerate nucleic acids do not teach variation from the Tek sequence at all. To the contrary, a degenerate sequence by definition maintains the encoded amino acid sequence. The passage cited by the examiner makes clear that the degenerate nucleic acids encode the same amino acid sequence (page 9, line 35). As for the soluble Tek polypeptides, multimers, Fc fusion molecules, and variants, they maintain all or a substantial portion of the Tek sequence. The examiner argued that:...[R]andomization would have been obvious to one having ordinary skill in the art in view of the teachings

of Cerretti of variants of the Ang-2 binding peptide i.e., Tek polypeptide, wherein one to ten amino acids are varied in a random manner. Such variations in the amino acids would suggest random amino acids. One having ordinary skill in the art would be motivated to randomized (sic) portions of the Ang-2 binding molecule (i.e., Tek). Randomization produces a diverse or more variants that leads to the discovery of lead compounds with better pharmacological effect. (Office Action at pages 9-10). This argument, however, appears to apply an "obvious to try" standard of obviousness, which has been explicitly rejected by the Court of Appeals for the Federal Circuit. In re O'Farrell, 853 F. 2d 894 (Fed. Cir. 1988).

In reply, degeneracy of genetic code do not maintain the encoded amino acid sequence. Rather, for a single code (codon) several amino acids are encoded. Randomization of the sequence is not "obvious try" because Cerretti positively teaches or at least suggests variations of amino acids. Randomization is nothing more than variations of amino acids in e.g., one or more positions that result in a variant(s) peptide sequence(s).

Applicants moreover argue that the randomized ang-2 binding peptides used in the claimed molecules have sequences that are not tied to the Tek sequence, as noted in the specification, they can result from such techniques as phage

display technology, which starts with a library of random sequences rather than variations from a known sequence having the desired activity. Finally, the Examiner's argument ignores that Cerretti et al. teach a limit of variation of 10 amino acids in the Tek polypeptide sequence. The soluble Tek polypeptide taught by Cerretti et al. has a sequence of hundreds of amino acids. So, in its teaching of variants, Cerretti et al. teach not only variation of up to 10 amino acids but also adherence to a sequence of hundreds of amino acids of the soluble Tek polypeptide. Thus, Cerretti et al. can be read as teaching away from the claimed invention, which relies on no adherence to the Tek sequence whatsoever.

In response, applicants did not specifically point out where in the specification the randomized ang-2 binding peptides is described. There is nothing in the claims to preclude the presence of other sequences attached to Ang-2 binding peptide. Applicants recognize that Cerrretti teach a limit of 10 amino acids in the Tek polypeptide sequence (which is within the claimed range of 2-40 residues). But argue that Cerretti is a teaching away because variation is not only on up to 10 residues but also to a sequence of hundreds of amino acids of the soluble Tek polypeptide. It matters not that Cerretti teaches variations

in hundreds of residues as Cerretti positively teaches 10 residues that is within the claimed range residues.

Newly added claims 63 and 64 are obvious over the teachings of Cerretti, which teaches or at least suggests phage display technique. [A product defined by the process by which it can be made is still a product claim (In re Bridgeford, 357 F.2d 679, 149 USPQ 55 (CCPA 1966))].

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
April 28, 2005